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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/977,716	10/15/2001	Mark I. Greene	UPN-5250	4425

23377 7590 10/03/2008

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EXAMINER	
TUNG, JOYCE	
ART UNIT	**PAPER NUMBER**
1637	

MAIL DATE	DELIVERY MODE
10/03/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/977,716	GREENE ET AL.	
	Examiner	Art Unit	
	Joyce Tung	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,15,16 and 18-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 15-16 and 18-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The applicant's response filed 6/30/08 to the office action has been entered. Claims 1, 15-16, 18-33 are pending.

1. Claims 1, 15-16, and 18-33 respectively remain rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 7,045,286, over claims 1-2, 4, and 12-18 of copending Application No. 10/856,057 and over claims 1-4 of copending Application No. 10/333542 as set forth in the office action mailed 9/21/06 because the terminal disclaimer was not filed.

2. Claims 1, 15-16 and 18-33 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Since the newly added phrase "unlabeled" to RNA product has no support in the specification, it constitutes new matter.

The response indicates the paragraph on pg. 11 lines 24-33 is support for the newly added phrase "unlabeled" amplified RNA product. However the paragraph describes a variety of means for detection of amplified products of the epitope detector. The paragraph does not state that the amplified RNA is unlabeled. Thus, the rejection is maintained.

3. Claims 1, 15-16 and 18-22 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Kacian et al. (5,888,729 issued Mar 30, 1999) in view of Eberwine et

al. (5,922,553, issued 7/13/1999), Fields et al. (WO 94/26932, issued November 24, 1994) and Waggoner (5,627,027, issued May 6, 1997).

Kacian et al. disclose a method for detecting and/or quantitating a specific nucleic acid target sequence in a sample (See column 3, lines 45-49). The method produces a RNA-promoter driven cDNA sequence, which is used to produce RNA copies (See column 4, lines 30-45 and column 9, lines 25-39).

Kacian et al. do not disclose the RNA-promoter driven cDNA, which is coupled, to an antibody for the protein detection or quantification by immuno aRNA.

Eberwine et al. disclose a method, which is for detecting a selected protein by immuno aRNA (See column, 2, lines, 37-50). The presence and quantity of labeled RNA transcript is indicative of the amount of selected protein present (See column 4, lines 33-36 and columns 7-8, claims 1-2). In the method, a first antibody targeted to the selected protein is immobilized to a solid support. A RNA-promoter driven cDNA sequence is covalently coupled to a second antibody, which binds to the selected protein (See column 2, lines 37-51). The cDNA is double stranded (See column 5, lines 34-35) for use as a template for T7 RNA polymerase (see column 4, lines 41-42). The technique of a RNA synthesis is explicitly disclosed (See column 3, lines 9-24). First strand synthesis proceeds with the addition of AMV-reverse transcriptase (See column 4, lines 50-51). The presence and quantity of labeled RNA transcript is indicative of the amount of selected protein present (See column 4, lines 33-36).

One of ordinary skill in the art would have been motivated to use the RNA-promoter driven cDNA as produced by the method of Kacian et al. to couple to an antibody because Eberwine et al. taught coupling the RNA-promoter driven cDNA to an

antibody (See column 5, lines 65-67 and column 6, lines 1-6) used in a method of immuno aRNA (See column 2, lines 44-50) and the RNA-promoter driven cDNA of Kacian et al. produces large number of RNA (See column 4, lines 30-45 and column 9, lines 25-39).

However, by using the method of Kacian et al. to produce RNA, the amplified RNA of Kacian et al. is unlabeled and Kacian et al. do not disclose using fluorescent dye to stain unlabeled amplified RNA and that the fluorescent dye is cyanine dye.

Waggoner discloses that cyanine dye can be used to attach to fragments of DNA or RNA to identify the presence and quantity of specific nucleotide sequence in samples of DNA or RNA (See column 8, lines 51-56).

One of ordinary skill in the art at the time of the instant invention would have been motivated to apply fluorescent dye, cyanine dye to stain the unlabeled amplified RNA of Kacian et al. for detecting and/or quantifying molecules expressing a selected epitope in a sample because as indicated by Waggoner, cyanine dye is highly light absorbing dye molecules to nucleic acid and can be used for detection and quantification in very low amounts (See column 4, lines 35-45) It would have been prima facie obvious to apply cyanine dye for detecting or quantifying molecule expressing a selected epitope in a sample.

Eberwine et al. and Kacian et al. also do not disclose that biotin is located at the 5' terminus of the oligonucleotide and biotin-streptavidin linker is used in attaching between monoclonal antibody and oligonucleotide.

Fields et al. disclose nucleic acid tagged immunoassay. The method involves an oligonucleotide linked to a ligand bound to an antigen in a specimen from a subject and

detecting the presence of the oligonucleotide indicating the presence of the antigen in the subject (See pg. 2, lines 14-25). Biotin-streptavidin linker is used in linking the oligonucleotide to the ligand (See pg. 5, lines 5-12). The oligonucleotide is amplified by polymerase chain reaction prior to detection (See pg. 5, lines 31-34). The oligonuleotide is biotinylated at 5' terminus (See pg. 15, lines 24-29). Other method of detecting the presence of the oligonucleotide includes the detection of RNA transcripts generated from the oligonucleotide using RNA polymerase (See pg. 6, lines 27-29).

One of ordinary skill in the art at the time of the instant invention would have also been motivated to apply the biotin-streptavidin as linker for attaching the oligonucleotide to the monoclonal antibody as taught by Fields et al. because the method of Fields et al. can be used in detecting very small quantities of antigen and antibody (See pg. 7, lines 22-25). It would have been prima facie obvious to apply the linker biotin-streptavidin for attaching the oligonucleotide to the monoclonal antibody for detecting or quantifying molecules expressing a selected epitope in a sample.

The response discusses the different interpretations between "stain" and "label" in which the phrases "stain" and "label" in the instant claims have their oridnary and customary meaning, which is reflected in the instant claims. However, the phrases "stain" and "label" do not have definitions in the specification. Nevertheless, the phrase "stain" is interpreted as set forth in the specification (See [0040] & [0041]) in which an unsymmetrical cyanine dye binds to RNA directly in the solution and then releases fluorescence signals. Waggoner discloses that cyanine dye can be used to attach to fragments of DNA or RNA to identify the presence and quantity of specific nucleotide sequence in samples of DNA or RNA (See column 8, lines 51-56).

The response further argues that the method of Kacian et al. detects amplified RNA with labeled probes; Eberwine et al. disclose labeled amplified RNA; combining the teachings of Eberwine et al. with Kacian et al. results in using unlabeled probe to detect labeled amplified RNA; the combination of the teachings does not teach or suggest: (a) detecting unlabeled amplified RNA and (b) staining techniques to detect unlabeled amplified RNA. However, the teachings of Kacian et al. and Eberwine et al. provided herein are because the method of Kacian et al. produces a RNA-promoter driven cDNA sequence, which is used to produce RNA copies (See column 4, lines 30-45 and column 9, lines 25-39) and Eberwine et al. disclose that a RNA-promoter driven cDNA sequence is covalently coupled to a second antibody, which binds a selected protein (See column 2, lines 37-51). Moreover it is true that the combination of the teachings does not teach or suggest: (a) detecting unlabeled amplified RNA and (b) staining techniques to detect unlabeled amplified RNA. As mentioned above, Waggoner discloses that cyanine dye can be used to attach to fragments of DNA or RNA to identify the presence and quantity of specific nucleotide sequence in samples of DNA or RNA (See column 8, lines 51-56). Regardless, using cyanine dye to stain fragments of DNA or RNA or to label a probe, Waggoner discloses that cyanine dye is a highly light absorbing dye molecule to nucleic acid and can be used for detection and quantification in very low amounts (See column 4, lines 35-45). It would have been prima facie obvious to apply cyanine dye to stain unlabeled amplified RNA for detecting molecules expressing a selected epitope in a sample.

Based upon the analysis above, the rejection is maintained.

Allowable Subject Matter

4. The following is a statement of reasons for the indication of allowable subject matter:

Concerning claims 23-33, no prior art has been found teaching or suggesting a method for quantifying molecules expressing a selected epitope in a sample comprising a step of measuring a quanta of fluorescence signals emitted from the stained amplified unlabeled RNA product which is directly proportional to epitope detector bound to the surface and molecules expressing the selected epitope in the sample.

There is no motivation to combine the cited references to achieve the step of measuring quanta of fluorescence signals emitted from stained unlabeled RNA product which is directly proportional to epitope detector bound to the surface and molecules expressing the selected epitope in the sample as required in claim 23.

Summary

5. No claims are allowed.

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the

advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (571) 272-0790. The examiner can normally be reached on Monday - Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kenneth R Horlick/
Primary Examiner, Art Unit 1637

Joyce Tung
September 18, 2008